

What is claimed is:

1. A receptor protein capable of binding a PACAP or a salt thereof.

2. The receptor protein of claim 1, wherein the receptor is endogenous to rat, bovine or human.

3. The receptor protein as claimed in claim 1 which comprises an amino acid sequence containing at least one member selected from the group consisting of the amino acid sequences of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11 and SEQ ID NO: 12 or a salt thereof.

4. The receptor protein as claimed in claim 1 which comprises an amino acid sequence containing the amino acid sequence of SEQ ID NO: 13 or a salt thereof.

5. The receptor protein as claimed in claim 1 which comprises an amino acid sequence having 90 to 100% homology as determined by sequence analysis with at least one member selected from the group consisting of the amino acid sequences of SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 24, SEQ ID NO: 26 and SEQ ID NO: 28 or a salt thereof.

6. The receptor protein as claimed in claim 1 which comprises an amino acid sequence selected from the group consisting of the amino acid sequences of SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18,

SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28 and SEQ ID NO: 29 or a salt thereof.

7. A receptor fragment containing a sufficient portion of the receptor of claim 1 to bind PACAP or a salt thereof.

8. The receptor fragment as claimed in claim 7 selected from the group consisting of

(1) peptides having the amino acid sequence consisting of the 38th to 164th, 223rd to 232nd, 303rd to 317th or 416th to 424th amino acid residues of SEQ ID NO: 15,

(2) peptides having the amino acid sequence consisting of the 38th to 164th, 223rd to 232nd, 303rd to 317th or 388th to 397th amino acid residues of SEQ ID NO: 17,

(3) peptides having the amino acid sequence consisting of the 20th to 146th, 205th to 214th, 286th to 299th or 369th to 378th amino acid residues of SEQ ID NO: 19,

(4) peptides having the amino acid sequence consisting of the 20th to 146th, 205th to 214th, 286th to 299th or 397th to 406th amino acid residues of SEQ ID NO: 21, and

(5) peptides having the amino acid sequence consisting of the 78th to 204th, 263rd to 272nd, 342nd to 357th or 427th to 436th amino acid residues of SEQ ID NO: 23; or a salt thereof.

9. An isolated DNA coding for a receptor protein

capable of binding a PACAP.

10. The DNA as claimed in claim 9 wherein the receptor protein comprises the amino acid sequence of SEQ ID NO: 14, SEQ ID NO 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO 18, SEQ ID NO: 19, SEQ ID NO 20, SEQ ID NO: 21, SEQ ID NO 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO 25, SEQ ID NO: 26, SEQ ID NO 27, SEQ ID NO: 28 or SEQ ID NO 29.

11. The DNA as claimed in claim 9 comprising the nucleotide sequence of SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO 35, SEQ ID NO: 36 or SEQ ID NO 37.

12. The DNA of claim 9 wherein the DNA is a cDNA.

13. A vector containing the DNA as claimed in claim 9.

14. A transformant containing the DNA as claimed in claim 9.

15. A method for preparing the receptor protein or the salt thereof as claimed in claim 1 comprising cultivating a transformant containing a DNA encoding said protein under conditions suitable for expression of said protein and recovering said protein.

16. A method for purifying the receptor protein or the salt thereof as claimed in claim 1 comprising subjecting a sample containing unpurified receptor protein to affinity chromatography using a biotinylated PACAP.

17. The method as claimed in claim 16 comprising the

steps of:

- (a) preparing a membrane protein fraction from an animal tissue or cell,
- (b) solubilizing the membrane protein fraction obtained in step (a),
- (c) subjecting the solubilized membrane protein fraction obtained in step (b) to anion exchange chromatography and/or hydroxyapatite chromatography, and
- (d) subjecting the active fraction obtained in step (c) to affinity chromatography using a biotinylated PACAP.

18. The method as claimed in claim 17, in which the animal tissue is a bovine cerebrum.

19. A method for preparing the receptor protein or the salt thereof as claimed in claim 1 comprising condensing a partial peptide fragment or a single amino acid corresponding to a portion of the protein as claimed in claim 1 with a residual moiety, and removing a protective group as so desired when the product has the protective group, until said protein is obtained.

20. A diagnostic composition for neuropathy comprising the PACAP receptor protein or the salt thereof as claimed in claim 1, or the receptor fragment or the salt thereof as claimed in claim 7.

21. The diagnostic composition as claimed in claim 20 which is a diagnostic composition for Alzheimer's disease.

22. A gene therapeutic composition comprising the DNA

as claimed in claim 9.

23. The gene therapeutic composition as claimed in claim 22 to be administered to a patient whose an amount of PACAP receptor protein is decreased, to increase the amount of PACAP receptor protein.

24. A method of diagnosis for neuropathy comprising contacting a sample to be tested with a receptor protein capable of binding a PACAP protein and measuring the amount of PACAP binding to the receptor protein.

25. The method of diagnosis of claim 24, wherein the receptor protein is a receptor fragment as claimed in claim 7.

26. The method as claimed in claim 24 wherein a decrease in PACAP concentration is an indication of the presence of Alzheimer's disease.

27. A method of using the DNA of claim 9 to transform a cell.

28. The method of claim 27 wherein the cell is transformed in vitro.

29. The method of claim 27 wherein the cell is transformed in vivo.

30. The method as claimed in claim 27, in which the expression of the DNA increases the amount of PACAP receptor protein.

31. A method for determining  
(i) an effect of a test compound on PACAP receptor activity

comprising comparing PACAP receptor activities in cases of

(a) and (b);

(a) contacting PACAP receptor with a PACAP;

(b) contacting PACAP receptor with a PACAP and a test compound, or

(ii) an effect of a test compound on binding of PACAP to PACAP receptor comprising comparing an amount of binding of PACAP to PACAP receptor in cases of (a) and (b);

(a) contacting PACAP receptor with a PACAP;

(b) contacting PACAP receptor with a PACAP and a test compound.

32. The method of claim 31 wherein the PACAP receptor is a protein as claimed in claim 1.

33. The method of claim 31 wherein the PACAP receptor is a receptor fragment as claimed in claim 7.

34. The method of claim 31 wherein the PACAP receptor is a protein produced by cultivating a transformant containing the DNA as claimed in claim 9.

35. The method of claim 31 which is a method for screening a compound activating PACAP receptor or a compound antagonizing binding of a PACAP to a PACAP receptor.

36. An assay for quantifying a test compound's effect  
(i) on PACAP receptor activity comprising comparing an amount of PACAP receptor activation in cases of (a) and (b);

- (a) contacting PACAP receptor with a PACAP;
- (b) contacting PACAP receptor with a PACAP and a test compound, or
- (ii) on binding of PACAP to PACAP receptor comprising comparing an amount of binding of PACAP to PACAP receptor in cases of (a) and (b);
- (a) contacting PACAP receptor with a PACAP;
- (b) contacting PACAP receptor with a PACAP and a test compound.

37. A compound or a salt thereof obtained by the method as claimed in claim 31.

38. The compound or a salt thereof as claimed in claim 37 which is a compound activating PACAP receptor or a compound antagonizing binding of a PACAP to a PACAP receptor.

39. A pharmaceutical composition for neuropathy comprising an effective amount of the compound or the salt thereof as claimed in claim 37.

40. The pharmaceutical composition of claim 39, wherein the neuropathy is Alzheimer's disease.

41. An antibody to a receptor protein capable of binding a PACAP, a partial peptide thereof or a salt thereof.

42. The antibody as claimed in claim 41 which is a monoclonal antibody selected from the group consisting of PRN1-25a, PRN1-109a and PRN1-159a.

43. Hybridoma which produces a monoclonal antibody as claimed in claim 42.

44. A signal peptide selected from the group of peptides consisting of a peptide which has 1st to 37th amino acid sequence of SEQ ID NO:15, a peptide which has 1st to 37th amino acid sequence of SEQ ID NO:17, a peptide which has 1st to 19th amino acid sequence of SEQ ID NO:19, a peptide which has 1st to 19th amino acid sequence of SEQ ID NO:21, a peptide which has 1st to 77th amino acid sequence of SEQ ID NO:23, a peptide which has 1st to 77th amino acid sequence of SEQ ID NO:25, a peptide which has 1st to 77th amino acid sequence of SEQ ID NO:27, a peptide which has 1st to 77th amino acid sequence of SEQ ID NO:29, a peptide which has 58th to 77th amino acid sequence of SEQ ID NO:23, a peptide which has 58th to 77th amino acid sequence of SEQ ID NO:25, a peptide which has 58th to 77th amino acid sequence of SEQ ID NO:27 and a peptide which has 58th to 77th amino acid sequence of SEQ ID NO:29; or a salt thereof.

45. A DNA which codes for a peptide as claimed in claim 44.

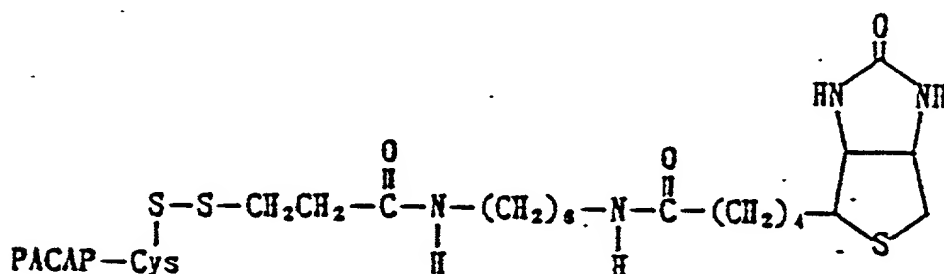
46. A DNA as claimed in claim 45 which is selected from the group consisting of a DNA which has 1st to 111th nucleotide sequence of SEQ ID NO:30, a DNA which has 1st to 111th nucleotide sequence of SEQ ID NO:31, a DNA which has 1st to 57th nucleotide sequence of SEQ ID NO:32, a DNA



which has 1st to 57th nucleotide sequence of SEQ ID NO:33, a DNA which has 1st to 231st nucleotide sequence of SEQ ID NO:34, a DNA which has 1st to 231st nucleotide sequence of SEQ ID NO:35, a DNA which has 1st to 231st nucleotide sequence of SEQ ID NO:36, a DNA which has 1st to 231st nucleotide sequence of SEQ ID NO:37, a DNA which has 172nd to 231st nucleotide sequence of SEQ ID NO:34, a DNA which has 172nd to 231st nucleotide sequence of SEQ ID NO:35, a DNA which has 172nd to 231st nucleotide sequence of SEQ ID NO:36 and a DNA which has 172nd to 231st nucleotide sequence of SEQ ID NO:37.

47. A biotinylated PACAP.

48. The biotinylated PACAP as claimed in claim 47 which is represented by the following formula:



49. The biotinylated PACAP as claimed in claim 47 or 48, in which the PACAP is PACAP27.

50. A method for preparing the biotinylated PACAP as claimed in claim 47 comprising reacting a PACAP derivative in which a cysteine residue is introduced into the carboxyl terminus of a PACAP with a biotinylating reagent.